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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/632,426	08/01/2003	Bernhard Kaltenboeck	35721/265190	4998
826	7590	03/25/2004	EXAMINER	
ALSTON & BIRD LLP BANK OF AMERICA PLAZA 101 SOUTH TRYON STREET, SUITE 4000 CHARLOTTE, NC 28280-4000			FIELD, TAMMY K	
		ART UNIT	PAPER NUMBER	
		1645		

DATE MAILED: 03/25/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)
	10/632,426	KALTENBOECK ET AL.
	Examiner Tammy K. Field	Art Unit 1645

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) Responsive to communication(s) filed on 24 November 2003.
- 2a) This action is FINAL. 2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) Claim(s) 1-9 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) Claim(s) _____ is/are allowed.
- 6) Claim(s) 1-9 is/are rejected.
- 7) Claim(s) 1c, 1d, 4 and 7 is/are objected to.
- 8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on _____ is/are: a) accepted or b) objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 - a) All b) Some * c) None of:
 1. Certified copies of the priority documents have been received.
 2. Certified copies of the priority documents have been received in Application No. _____.
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ . |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>10/31/03</u> . | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| | 6) <input type="checkbox"/> Other: _____. |

DETAILED ACTION

1. Claims 1-9 are presently under examination.

Priority

2. Applicant's claim for domestic priority to provisional 60/401,070 under 35 U.S.C. 119(e) is acknowledged.

Information Disclosure Statement

3. The information disclosure statement(s) filed October 31, 2003 has been considered. An initialed copy is enclosed.

Specification

4. The disclosure is objected to because of the following informalities:
 - a. The specification discloses 11 nucleic acid sequences at pages 20-21 and two nucleic acid sequences at page 28 that appear to be critical or essential to the practice of the invention. Applicant is required to amend the specification to indicate the SEQ ID: # for each disclosed nucleic acid sequence received in the sequence listing in which Error(s) in CRF were corrected by STIC on August 19, 2003 and then, received by OIPE November 24, 2003.
 - b. The lengthy specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification. Appropriate correction is required.

Claim Objections

5. Claim 1d, 4, and 7 are objected to because of the following informalities:
- c. The abbreviations “NOS2” (claim 1d), “NO” (claim 4) and “AG” (claim 7) should completely spelled out initially when introduced in claim language and then followed by abbreviation if used in subsequent claims.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 1-9 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of evaluating the efficacy of Chlamydia-induced disease by varying the levels of NOS2 inhibitor or arginine in a mouse diet, does not reasonably provide enablement for a method of evaluating the efficacy of therapeutic or prophylactic treatment of Chlamydia-induced disease. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The claims encompass a method of evaluating the efficacy of therapeutic or prophylactic treatment of Chlamydia-induced disease comprising: a) rationally selecting a test mouse, b) rationally selecting a dose of Chlamydia for administration, c) optionally, rationally selecting a feeding regimen, d) optionally treating with a NOS2 inhibitor, e) administering Chlamydia to mouse, f) administering said therapeutic or prophylactic treatment, and g) assessing the severity of Chlamydia disease in said test mouse. Subsequent claims encompass administering prophylactic treatment before administering Chlamydia, dosages of Chlamydia for administration, testing for macrophage NO production, feeding regimens of Arginine in diet, AG as NOS2 inhibitor, selecting a mouse strain which has a high NO response, and evaluating mouse strains.

The teachings of the specification appear to disclose AG as the only therapeutic or prophylactic treatment in a method of evaluating the efficacy of a therapeutic or prophylactic treatment of Chlamydia-induced disease. The specification is silent to any other therapeutic or prophylactic treatments, *e.g.* antibiotics or preventive vaccines, either before or after administering Chlamydia to mice.

Campbell, L.A. *et al.* 1998. (*Clin. Microbial. Infect.* 4(supp. 4): S23-S32) teach the efficacy of roxithromycin pretreatment and post-treatment in Chlamydia induced-infection with a mouse model as measured by Chlamydia % positive mice at page 4S29 (see Table 7). Campbell, L.A. *et al.* further teach evaluation of the susceptibility of *C. pneumoniae* to roxithromycin *in vivo* in the apoE-deficient mouse model compare favorably with quinolines, and tetracycline (see Abstract and Discussion at 4S30).

The specification discloses evaluating Chlamydia induced-disease. It appears a NOS2 inhibitor, more specifically AG, is the only therapeutic or prophylactic treatment disclosed. Thus, it is unclear how NOS2 inhibitors and feeding regiments high in Arginine are effective in the assessment of other therapeutic or prophylactic treatments of Chlamydia disease. Without further direction from the applicant's disclosing the efficacy of known therapeutic or prophylactic treatments for Chlamydia as they relate to diet regimens of arginine, it would cause undue burden on one of skill in the art to which it pertains, or with which it is most nearly connected, to practice the invention as claimed. Therefore, in view of the evidence presented supra, it is determined that while the specification is enabled for a method of evaluating the efficacy of Chlamydia-induced disease by varying the levels of NOS2 inhibitor or arginine in a mouse diet, does not reasonably provide enablement for a method of evaluating the efficacy of therapeutic or prophylactic treatment of Chlamydia-induced disease.

7. Claim 1 c) and 1d) is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The language of the claims is not as precise as the subject matter permits such that one may reasonably know the metes and bounds of the claims and bounds of the claimed subject matter. The claims are indefinite in the recitation of "optionally" because it is unclear from the specification what applicant intends. Clarification is required in order to overcome this rejection.

Claim Rejections - 35 USC § 102 and 103

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

- (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
- (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

- (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

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8. Claims 1-9 are rejected under 35 U.S.C. 102(a) as being anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Huang, J. *et al.* 2002. (PNAS v99(6)3914-3919).

The claims are drawn to a method of evaluating the efficacy of therapeutic or prophylactic treatment of Chlamydia-induced disease comprising: a) rationally selecting a test mouse, b) rationally selecting a dose of Chlamydia for administration, c) optionally, rationally selecting a feeding regimen, d) optionally treating with a NOS2 inhibitor, e) administering Chlamydia to mouse, f) administering said therapeutic or prophylactic treatment, and g) assessing the severity of Chlamydia disease in said test mouse. Subsequent claims are drawn to administering prophylactic treatment before administering Chlamydia, dosages of Chlamydia for administration, testing for macrophage NO production, feeding regimens of Arginine in diet, AG as NOS2 inhibitor, selecting a mouse strain which has a high NO response, and evaluating mouse strain.

Huang, J. *et al.* teach selecting mice [Harlan Sprague-Dawley; NO synthase 2 (NOS2)-/- and NOS2+/+ of C57BL/6 control mice, The Jackson Laboratory] and BALB/c mice (see Material and Methods). Huang, J. *et al.* also teach mice were fed 1.33% L-arginine in rodent chow and drinking water with L-norvaline thereby affecting NO production with arginase and NOS2 inhibitors, inherently rationally selecting a feeding regimen (Materials and Methods and page 3917, paragraph 3 and Fig. 3A). Huang, J. *et al.* further teach selecting dose levels of (0.3-8.1 X 10⁵ IFC *C. psittaci*) for C57Bl/6 mice at Results, page 3915. Huang, J. *et al.* further teach aminoguanidine (AG)-treated mice received 2 i.p. injections/day (Materials and Methods) and the kinetics of Chlamydia pneumonia under AG influence of C57BL/6 mice treated with 6 mg

AG/kg per day were protected from disease at page 3917 (see Fig. 5). Huang, J. *et al.* further teach regarding macro-released NO synthesized by NOS2, C57BL/6 mice produced significantly more NO than BALB/c mice at all time points after infection at Results page 3915 (see Fig. 1F). Huang, J. *et al.* also teach at high dose inoculation, some BALB/c mice developed lethal disease after 7 days, inherently a lethal dose, *i.e.* LD₅₀ (see Materials and Methods). As such, the method of Huang, J. *et al.* does not provide any distinguishing features from the instant method of evaluating the efficacy of a therapeutic or prophylactic treatment of Chlamydia-induced disease. Therefore, the method of the prior art is inherently the same

In the alternative, while Huang, J. *et al.* does not teach the limitation of claim 2 their findings teach genetically determined regulation of macrophage NO production in inbred mice suggests (emphasis added) that similar high and low NO responder genotypes with differential susceptibility to chlamydial disease may exist in the human population (see Discussion at page 3919, paragraph 1). The motivation for doing what Applicants have claimed is present in the methods of the prior art as taught by Huang, J. *et al.* because one would want to administer a prophylactic treatment (*e.g.* vaccine) prior to infecting with Chlamydia. Thus, it would have been *prima facie* obvious to one having ordinary skill in this art at the time the invention was made to use the instant method in evaluating the efficacy of therapeutic or prophylactic treatment of Chlamydia-induced disease.

Thus, Huang, J. *et al.* anticipates or, in the alternative is obvious over the instantly claimed method.

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9. Claims 1and 2 are rejected under 35 U.S.C. 102(b) as being anticipated by Campbell *et al.* 1998. (*Clin. Microbiol. Infect.* v4(Supp. 4): S23-S32).

The claims are drawn to a method of evaluating the efficacy of therapeutic or prophylactic treatment of Chlamydia-induced disease comprising: a) rationally selecting a test mouse, b) rationally selecting a dose of Chlamydia for administration, c) optionally, rationally selecting a feeding regimen, d) optionally treating with a NOS2 inhibitor, e) administering Chlamydia to mouse, f) administering said therapeutic or prophylactic treatment, and g) assessing the severity of Chlamydia disease in said test mouse. Subsequent claims are drawn to administering prophylactic treatment before administering Chlamydia, dosages of Chlamydia for administration, testing for macrophage NO production, feeding regimens of Arginine in diet, AG as NOS2 inhibitor, selecting a mouse strain which has a high NO response, and evaluating mouse strain.

Campbell *et al.* teach rationally selecting Apo-E-deficient C57BL/6J mice obtained from Jackson Laboratories and inoculating with 3-5 X10⁷ IFUs at page 4S24 (Inoculation of mice). Campbell *et al.* further teach intranasal inoculation of Apo-E-deficient mice at page 4S26 (see Roxithromycin treatment). Campbell *et al.* further teach assessing the efficacy of Roxithromycin treatment in chronic *C. pneumonia* infection for pretreatment and post-treatment of test mice at page 4S29 (see Susceptibility of *C. pneumonia* to Roxithromycin and Table 7).

Thus, Campbell *et al.* anticipates the instantly claimed invention.

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10. Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by Yang, Z. *et al.* 1993. (Infect. Immun. v4(Supp. 4): S23-S32).

The claims are drawn to a method of evaluating the efficacy of therapeutic or prophylactic treatment of Chlamydia-induced disease comprising: a) rationally selecting a test mouse, b) rationally selecting a dose of Chlamydia for administration, c) optionally, rationally selecting a feeding regimen, d) optionally treating with a NOS2 inhibitor, e) administering Chlamydia to mouse, f) administering said therapeutic or prophylactic treatment, and g) assessing the severity of Chlamydia disease in said test mouse. Subsequent claims are drawn to administering prophylactic treatment before administering Chlamydia, dosages of Chlamydia for administration, testing for macrophage NO production, feeding regimens of Arginine in diet, AG as NOS2 inhibitor, selecting a mouse strain which has a high NO response, and evaluating mouse strain.

Yang, Z. *et al.* teach a mouse model of pneumonitis that should be useful for studying the pathogenesis of *C. pneumoniae* and outbred mice (Swiss Webster and Icr), inbred mice (BALB/cAnN, C57BL/6N and C3H/HeN), and hybrid mice (B6C3F₁) (Simonsen Laboratory Company, Gilroy, Calif.), *i.e.* test mice, were used and inoculated with *C. pneumoniae* (see Introduction, 4th paragraph and Material and Methods). Yang, Z. *et al.* further teach determination of susceptibilities in test mice (Results and Table 1).

Thus, Yang, Z. *et al.* anticipates the instantly claimed invention.

Since the office does not have the facilities for examining and comparing applicants' methods with the methods disclosed in the prior art, the burden is on applicant to show a novel or unobvious difference between the claimed method and the methods of the prior art (*i.e.* that the

methods of the prior art does not possess the same material structural and functional characteristics of the claimed methods). See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

Status of the Claims

11. No claims allowed.

Conclusion

12. The prior art of record and not relied upon is considered pertinent to applicant's disclosure:

- (a) Igietseme, J.U. *et al.* 1997. (Biochem. Biophys. Res. Comm. 232: 595-601) teach NO could directly inhibit human strains of Chlamydia.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Tammy K. Field whose telephone number is (571) 272-0856. The examiner can normally be reached on Monday-Friday from 7am-4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached at (571) 272- 0864.

Papers relating to this application may be submitted to Technology Center 1600 Group 1640 by facsimile transmission. The faxing of such papers must conform to the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306 for regular communications and After Final communications.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov/>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Tammy K. Field
March 19, 2004



MARK NAVARRO
PRIMARY EXAMINER